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09/904,766	07/12/2001	Avi Ashkenazi	10466/70	4054

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EXAMINER	
ROARK, JESSICA H	
ART UNIT	PAPER NUMBER
1644	20

DATE MAILED: 06/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/904,766	Applicant(s) ASHKENAZI ET AL.
	Examiner Jessica H. Roark	Art Unit 1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 February 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *39-46 and 49-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39-46 and 49-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 February 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *17* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 2/21/03 (Paper No. 14), is acknowledged.
Claims 47 and 48 have been cancelled. Claims 1-38 have been cancelled previously.
Claims 39-44 have been amended.
Claims 39-46 and 49-51 are pending and are under consideration in the instant application.

2. This Office Action will be in response to applicant's arguments, filed 2/21/03 (Paper No. 14). The rejections of record can be found in the previous Office Action (Paper No. 11).

It is noted that New Grounds of Rejection are set forth herein.

3. Applicant's cancellation of claims 47 and 48 has obviated the previous objections and rejections with respect to these claims.

Objections not reiterated may be considered obviated by Applicant's amendment, filed 2/21/03.

Drawings

4. The formal drawings filed 2/21/03 have been found acceptable by the Draftsman.

Priority

5. Applicant's comments, filed 2/21/03, regarding the priority claimed in the instant application are acknowledged.

Applicant argues that the claims as amended do have a specific and substantial utility and therefore are entitled to an effective filing date of Feb. 11, 2000 because the results providing utility were first disclosed in PCT/US00/03565.

For the reasons addressed in detail below in the rejections under 35 USC 101, Applicant's arguments that the invention as now claimed has a specific and substantial utility are not found convincing. It is further noted that priority requires adequate written description under 35 USC 112.

Accordingly, the subject matter defined in claims 39-46 and 49-51 appears to have an effective filing date of 7/12/01.

IDS

6. Applicant's supplemental IDS, filed 2/21/03, is acknowledged. However, GenBank CNSLT1I5k (IDS #11) and GenBank CNSO7EEV (IDS#12) were not found as part of the references and therefore have not been considered.

Claim Rejections - 35 USC § 101

7. 35 U.S.C. § 101 reads as follows:

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

8. Claims 39-46 and 49-51 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility.

Applicant's arguments with respect to the asserted utility of PRO269 as a diagnostic marker for lung cancer, filed 2/21/03, have been fully considered but have not been found convincing.

The rejection of record in full may be found in Paper No. 11. The asserted utility of a diagnostic marker for lung tumors does not appear to affect the Examiner's previous comments with respect to other asserted utilities, which may be found in full in Paper No. 11.

Applicant argues in the Remarks filed 2/21/03 that PRO269 showed approximately 2-3 fold amplification in 8 primary lung tumors and asserts that PRO269 therefore has a specific, substantial and credible use as a diagnostic marker for lung cancer.

Applicant provides in support of this assertion a Declaration under 37 CFR 1.132 by Dr. Goddard supporting that the TaqMan PCR technique is technically sensitive enough to detect at least a 2-fold increase in gene copy number relative to control. Dr. Goddard concludes that a gene identified as being amplified at least 2-fold by the quantitative TaqMan PCR assay in a tumor sample relative to a normal sample is useful as a marker for the diagnosis of cancer, for monitoring cancer development and/or for measuring the efficacy of cancer therapy.

It is noted that a second, unexecuted Declaration under 37 CFR 1.132 by Dr. Goddard was also filed on 2/21/03. Since the Declaration was not executed, statements therein cannot be found convincing. However, it is noted that similar arguments are advanced, but 4-fold, rather than 2-fold amplification of a gene is described as "significant".

As discussed in Applicant's Remarks filed 2/21/03, a 2 fold amplification corresponds to a ΔCt value of 1 unit. ΔCt values of 2 units correspond to a 4-fold amplification.

While the Examiner acknowledges that the results shown in Table 9 do show that the PRO269 gene had a ΔCt value of above 1 in 8 primary lung tumors, the PRO269 gene was not detected in 9 other primary lung tumors. In addition, the ΔCt values for the PRO269 gene were all less than 2 units, and most were close to 1 ΔCt. It appears form the discussion on page 22 of the disclosure (e.g., lines 11-32) that a CT value of +/- 1 identifies "background" of normal human DNA compared to the test DNA. Thus the significance of a ΔCt that close to 1 is far from clear.

Further, the amplification assays do not appear to control for aneuploidy. The data do not appear to be supported by analysis of mRNA or protein expression. A slight amplification of a gene in a cancer tissue does not necessarily mean that the gene is overexpressed: rather it may simply indicate that the cancer tissue is aneuploid (see e.g., Sen Curr. Opin. Oncol. 2000; 12:82-88).

Thus in view of ΔCt values that are only slightly above 1, the absence of any signal in as many primary lung tumors as were found to have a ΔCt above 1, and the absence of appropriate controls for the aneuploidy of the samples; the totality of the evidence does not support Applicant's assertion that one of skill in the art would find it more likely than not that PRO269 was a diagnostic marker for lung cancer.

The Examiner therefore maintains that at present the instant disclosure fails to clearly establish how one of skill in the art could use the claimed invention in a way that constitutes a credible specific and substantial utility. The disclosed modest increase of gene expression in a limited number of lung tumors for which aneuploidy was not assessed appears only to provide a starting point for further research and investigation into potential practical uses of the claimed PRO269 gene. In addition, the instant claims are drawn to a polypeptide and even were a diagnostic utility established for the gene, it is unclear whether a specific and substantial utility for the polypeptide would follow.

Applicant is again directed to the Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday January 5, 2001.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 39-46 and 49-51 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Applicant's arguments, filed 2/21/03, and the Examiner's comment with respect to the amended claims and the asserted utility of PRO269 as a diagnostic marker for lung cancer have been addressed supra.

11. The PRO269 polypeptide of SEQ ID NO:96 itself does not appear to be enabled for the reasons set forth supra. However, even were sufficient objective evidence provided that the PRO269 polypeptide of SEQ ID NO:96 were enabled for one or more of the asserted uses, the following rejections would still apply:

A) Claims 39-46 and 49-51 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

Even were the PRO269 gene found to be diagnostic of lung cancer, as asserted by Applicant in the response filed 2/21/03, the asserted use of the PRO269 polypeptide is for tumor therapy and is based on the preparation of antibodies to PRO269 and their use as antagonists of the PRO269 polypeptide (see e.g., page 235, lines 1-3 in view of the DNA amplification results on pages 222-234).

Applicant's arguments, filed 2/21/03 regarding the TaqMan PCR assay for detecting increased gene expression do not appear to address how increased amplification of the PRO269 gene, even were it found to be diagnostic for lung tumors, would provide sufficient guidance to the skilled artisan as to how to use the PRO269 protein.

Applicant does not appear to address the arguments present in the rejection of record in Paper No. 11 regarding insufficient guidance as to how to use the instantly recited protein, even were the protein found to be overexpressed in lung tumors.

B) Claims 39-43 and 50-51 are also rejected under 35 U.S.C. 112, first paragraph, because the specification, *even were it shown to be enabling* for the PRO269 polypeptide of SEQ ID NO:96, *still would not* reasonably provide enablement for polypeptides having less than 100% identity to at least the extracellular domain of SEQ ID NO:96. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant's response filed 2/21/03 does not appear to address the rejection of record in Paper No. 11 for how to make and use PRO269 polypeptides having less than 100% identity to SEQ ID NO:96.

The amendment filed 2/21/03 to require that the polypeptide is overexpressed in lung tumors does not appear to provide a meaningful limitation. There does not appear to be any working examples establishing that the PRO269 polypeptide of SEQ ID NO:96 is itself overexpressed in lung tumors: increased gene levels do not necessarily indicate increased expression of the protein. In addition, insufficient guidance is provided with respect to which structural aspects of SEQ ID NO:96 would contribute to overexpression in lung tumors.

The instant claims still do not require the PRO269 polypeptide variants share any testable function with PRO269. Neither does the specification appear to provide sufficient guidance as to which amino acids of PRO269 are essential to any of the functions ascribed to the PRO269 polypeptide. Such guidance requires knowledge as to which encoded amino acids actually contribute to particular functions versus which encoded amino acids are non-essential to those functions. The instant specification does not appear to provide this knowledge and guidance with respect to an assignment of function to specific amino acids.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. Without sufficient guidance, the changes which can be made in the PRO269 polypeptide and still maintain the assayable activities disclosed are unpredictable; thus the experimentation left to those skilled in the art, is unnecessarily, and improperly, extensive and undue.

The rejections of record are therefore maintained.

12. Claims 39-43 and 50-51 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The following *Written Description* rejection is set forth herein.

Applicant's arguments, filed 2/21/03, in view of the amendment also filed 2/21/03, have been fully considered but have not been found convincing.

Applicant asserts in the Remarks filed 2/21/03 that by amending the claims to require that the variant polypeptides are overexpressed in lung tumors, the instant claims provide a correlation between a structure and a function.

The instant claims are drawn to a genus of polypeptides related to the PRO269 polypeptide of SEQ ID NO:96. Applicant's assertion with respect to overexpression of the gene encoding the PRO269 polypeptide has been addressed supra. The ordinary artisan would not consider it more likely than not that the gene encoding PRO269 was overexpressed in a representative number of lung tumors in view of the evidence of record. As also noted supra, even were the gene overexpressed, protein overexpression is a separate issue for which there also does not appear to be evidence of record to support.

Applicant has disclosed a single polypeptide which itself does not appear to be significantly overexpressed in a representative number of lung tumors. Applicant does not appear to have established any correlation between the structure of the single species disclosed and overexpression in lung tumors.

Therefore, the Examiner maintains that even in view of the newly added limitation, only isolated polypeptides comprising the amino acid sequence set forth in SEQ ID NO: 96, but not the full breadth of the instant claims meets the written description provision of 35 U.S.C. 112, first paragraph.

Applicant is again directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The rejection is therefore maintained with respect to the amended claims.

13. In view of the amendment filed 2/21/03 clarifying the nature of the agreement between Genentech Inc. and the ATCC and providing the necessary assurances, the previous rejection of claims 39-44 and 49-51 under 35 U.S.C. 112, first paragraph, deposit, has been obviated.

14. Applicant's amendment, filed 2/21/03, has obviated the previous rejection of claims 39-44, 48 and 50-51 under 35 U.S.C. 112, second paragraph, as being indefinite.

Claim Rejections – 35 U.S.C. § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:
A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claims 39-46 and 49-51 are rejected under 35 U.S.C. 102(b), *or in the alternative under 35 U.S.C. 102(a)*, as being anticipated by Wood et al. (WO 99/14328, see pages 1, 12, 39, 56, 72, 83-85, 92-98, 101, 108-112, 126-127, 185-187, Figures 35 and 36, of record), as evidenced by the attached alignment "D".

Applicant's arguments, filed 2/21/03, have been fully considered but have not been found convincing.

Applicant' argues that the instant claims are entitled to an effective filing date of February 11, 2000.

For the reasons set forth supra, Applicant's argument with respect to the effective filing date of the instant claims has not been found convincing.

Applicant also argues that In re Wilder 166 USPQ 545 (C.C.P.A. 1970) invalidates Wood et al. as a reference because the instant claims recite properties completely different from those attributed to them by Wood et al.

However, a chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

It is noted that the Court in In re Wilder also appreciated that when the identical compound was described in the prior art, the evidence "quite reasonably also permits the inference that the reference patentee might only have been unaware of a particular property of the compound he did disclose. Such proof clearly falls short of defeating a case of anticipation." In re Wilder 166 USPQ 545, 549 (C.C.P.A. 1970).

The teachings of Wood et al. may be found in full in Paper No. 11. Wood et al. teach an isolated PRO269 polypeptide having the amino acid sequence of SEQ ID NO:96 as shown in Figure 36. The PRO369 polypeptide has 100% amino acid sequence identity to the amino acid sequence of the PRO269 polypeptide shown in Figure 36 (SEQ ID NO:96) of the instant application, as evidenced by the attached alignment.

The newly recited limitation of overexpression in lung tumors, if a property of the PRO269 polypeptide of SEQ ID NO:96, must also be an inherent property of the PRO269 polypeptide of Wood et al. in view of the identical amino acid sequence.

The reference teachings thus anticipate the instant claimed invention.

The rejection is therefore maintained.

17. Claims 39-46 and 49-51 are rejected under 35 U.S.C. 102(b) as being anticipated by Valenzuela et al. (WO 00/11015, see pages 1-2, 115-118, 167-168, 171-176, 183-184, 207-209 and pages 68-70 of the sequence listing, of record), as evidenced by the attached alignment "E".

Applicant's arguments, filed 2/21/03, have been fully considered but have not been found convincing.

Applicant' argues that the instant claims are entitled to an effective filing date of February 11, 2000.

For the reasons set forth supra, Applicant's argument with respect to the effective filing date of the instant claims has not been found convincing.

Valenzuela et al. teach an isolated vp15_1 polypeptide having the amino acid sequence of SEQ ID NO:72 (see e.g., pages 68-70 of the sequence listing). The vp15_1 polypeptide has 100% amino acid sequence identity to the amino acid sequence of the polypeptide shown in Figure 36 (SEQ ID NO:96), as evidenced by the attached alignment, and therefore anticipates section (a) of instant claims 39-44 and claim 45. With respect to section (e) of the instant claims 39-44, as well as claim 49; the polypeptide encoded by the cDNA deposited under ATCC accession number 209397 is the same as the full length of instant SEQ ID NO:96, and is therefore also anticipated by the teachings of the vp15_1 polypeptide.

Valenzuela et al. also teach the mature vp15_1 protein at page 167, lines 10-12, lacking the associated signal peptide, and therefore anticipate section (b) of instant claims 39-44 and 46.

Valenzuela et al. also teach chimeric polypeptides in which the vp15_1 polypeptide is fused to a heterologous polypeptide that is a epitope tag (page 184, lines 25-34) and therefore anticipate instant claims 50-51.

The newly recited limitation of overexpression in lung tumors, if a property of the PRO269 polypeptide of SEQ ID NO:96, must also be an inherent property of the vp15_1 polypeptide of Valenzuela et al. in view of the sequence identity of the prior art polypeptide and PRO269.

The reference teachings thus anticipate the instant claimed invention.

The rejection is therefore maintained.

Conclusion

18. No claim is allowed.

19. Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica Roark, whose telephone number is (703) 605-1209. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

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May 30, 2003

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